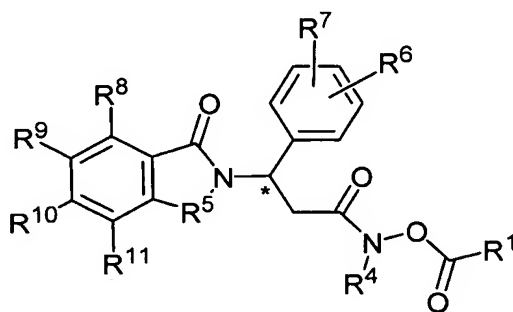


Amendments to the Claims

The following listing of claims will replace all prior versions and listings of claims in this application.

1. (Previously presented) A pharmaceutical composition comprising:
(a) a compound of the formula:



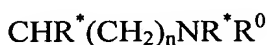
or an acid addition salts thereof,

wherein

the carbon atom designated * constitutes a center of chirality,

R⁴ is hydrogen or -(C=O)-R¹²;

each of R¹ and R¹², independently of each other, is alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridyl methyl, pyridyl, imidazolyl, imidazolylmethyl, or



wherein R^{*} and R⁰, independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazolyl or imidazolylmethyl, and n = 0, 1, 2;

R⁵ is C=O, CH₂, -CH₂-CO-, or SO₂;

each of R⁶ and R⁷, independently of the other, is nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxo, carboxy, hydroxy, amino, alkyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, cycloalkoxy of 3 to 8 carbon atoms, halo, bicycloalkyl of up to 18 carbon atoms, tricycloalkoxy of up to 18 carbon atoms, 1-

indanyloxy, 2-indanyloxy, C₄-C₈-cycloalkylidenemethyl, or C₃-C₁₀-alkylidenemethyl; and

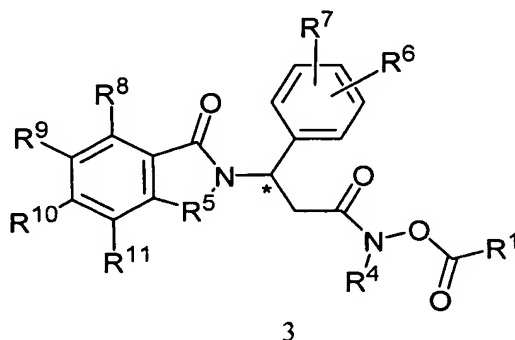
each of R⁸, R⁹, R¹⁰, and R¹¹ independently of the others, is

- (i) hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxyl, carboxyl, hydroxyl, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, halo, or
 - (ii) one of R⁸, R⁹, R¹⁰, and R¹¹ is acylamino comprising a lower alkyl, and the remaining of R⁸, R⁹, R¹⁰, and R¹¹ are hydrogen, or
 - (iii) hydrogen if R⁸ and R⁹ taken together are benzo, quinoline, quinoxaline, benzimidazole, benzodioxole, 2-hydroxybenzimidazole, methylenedioxy, dialkoxy, or dialkyl, or
 - (iv) hydrogen if R¹⁰ and R¹¹, taken together are benzo, quinoline, quinoxaline, benzimidazole, benzodioxole, 2-hydroxybenzimidazole, methylenedioxy, dialkoxy, or dialkyl, or
 - (v) hydrogen if R⁹ and R¹⁰ taken together are benzo; and
- (b) a pharmaceutically acceptable carrier.

2-4. (Canceled).

5. (Currently amended) A pharmaceutical composition comprising:

(a) a compound of the formula:



or an acid addition salt thereof,

in which

the carbon atom designated * constitutes a center of chirality;

R^4 is hydrogen or $-(C=O)-R^{12}$, where

each of R^1 and R^{12} , independently of each other, is alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridyl, pyridyl methyl, imidazolyl, imidazoylethyl, or $CHR^*(CH_2)_nNR^*R^0$

wherein R^* and R^0 , independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazolyl or ~~imidazolethyl~~ imidazolethyl, and $n = 0, 1, 2$;

R^5 is $C=O$ or CH_2 ;

each of R^6 and R^7 , independently of the other is alkoxy of 1 to 8 carbon atoms, cycloalkoxy of 3 to 6 carbon atoms; C_4-C_6 -cycloalkylidenemethyl, C_2-C_{10} -alkylidenemethyl, C_6-C_{18} -bicycloalkoxy, C_6-C_{18} -tricycloalkoxy, 1-indanyloxy, or 2-indanyloxy;

each of R^8 , R^9 , R^{10} , and R^{11} , independently of the others, is hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, halo, carbamoyl, acetoxyl, carboxyl, hydroxyl, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, and alkoxy of 1 to 10 carbon atoms; and

(b) a pharmaceutically acceptable carrier.

6-18. (Canceled).

19. (Currently amended) The pharmaceutical composition of claim 1, wherein said compound is a substantially chirally pure (R)-isomer, or a substantially chirally pure (S)-isomer, ~~or a mixture thereof, and wherein the composition is useful for reducing or inhibiting levels of TNF α , PDE 4 or matrix metalloproteinases in a mammal.~~

20-29. (Canceled).

30. (Currently amended) The pharmaceutical composition of claim 5, wherein said compound is a substantially chirally pure (R)-isomer, or a substantially chirally pure (S)-isomer, ~~or a mixture thereof, wherein the composition is useful for reducing or inhibiting the levels of TNF α , PDE 4 or a matrix metalloproteinase in a mammal.~~

31-40. (Canceled).

41. (New) The pharmaceutical composition of claim 1 or 5, wherein the compound is (3-(1,3-dioxoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino)propanoate; (3-(1,3-dioxoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino)acetate; (3-(1,3-dioxoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino)pentanoate; (3-(1,3-dioxoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino)benzoate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(1-oxoisindolin-2-yl)propanoylamino)acetate; (3-[4-(acetylamino)-1,3-dioxoisindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propanoylamino)acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisindolin-2-yl)propanoylamino)acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisindolin-2-yl)propanoylamino)acetate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisindolin-2-yl)propanoylamino)acetate; (3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisindolin-2-yl)propanoylamino)acetate; N-acetyl-(3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisindolin-2-yl)propanoylamino)acetate; N-acetyl-(3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(4-methyl-1,3-dioxoisindolin-2-yl)propanoylamino)acetate; (3-[5-(acetylamino)-1,3-dioxoisindolin-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propanoylamino)acetate; (3-(1,3-dioxobenzo[e]isindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino)acetate; (3-(3-ethoxy-4-methoxyphenyl)-3-phthalimido-propanoylamino)pyridine-3-carboxylate; (3-[4-(acetylamino)-1,3-dioxoisindolin-2-yl]-3-(3-cyclopentyloxy-4-methoxyphenyl)propanoylamino)acetate; (N-acetyl-3-[4-(acetylamino)-1,3-dioxoisindolin-2-yl]-3-(3-cyclopentyloxy-4-methoxyphenyl)propanoylamino)acetate; or (3-(3-ethoxy-4-methoxyphenyl)-3-(1-oxoisindolin-2-yl)propanoylamino)acetate.

42. (New) The pharmaceutical composition of claim 41, wherein the compound is a substantially chirally pure (R)-isomer or a substantially chirally pure (S)-isomer.